



PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Charles L. Magness and Shawn P. Iadonato
 Application No. : 09/707,576
 Filed : November 6, 2000
 For : SYSTEM AND METHOD FOR SELECTIVELY CLASSIFYING
 A POPULATION

Examiner : Anna Skibinsky
 Art Unit : 1631
 Docket No. : 55382-3
 Date : February 24, 2006

Mail Stop Amendment
 Commissioner for Patents
 P.O. Box 1450
 Alexandria, VA 22313-1450

Affidavit of Shawn Iadonato, Ph.D. under 37 C.F.R. § 1.132

I, Shawn Iadonato, Ph.D. being duly sworn, say:

1. I am an internationally recognized scientist and at the time of filing the above-referenced patent application I was employed as Vice-President and Chief Scientific Officer, at Illumigen Biosciences, Inc., Seattle, WA. I received a Bachelors Degree in Biology from the University of Pennsylvania in Philadelphia and a Ph.D. degree from in Genetics from the University of Washington.

2. I am an author or co-author of numerous peer-reviewed research articles and have been invited to give numerous presentations on my research at national and international meetings. Prior to joining Illumigen, I managed sequence data collection

for the University of Washington Genome Center. My curriculum vitae is attached as Exhibit 1.

3. In my capacity as Founder, Vice-President, and Chief Scientific Officer, I manage the scientific and drug development programs of Illumigen. I have more than eight years experience developing and managing large-scale genetics and genomics projects, most notably involving my work on the Human Genome Project.

4. On information and belief, claims of the present application have been rejected under 35 U.S.C. § 112, first paragraph. According to the Office Action dated September 29, 2005, claims 1-10, 14-26, 28, 31-44 and 46-55 fail to comply with the enablement requirement because allegedly there is “undue experimentation required to go from the classification results achieved by implementing the invention to drug target identification without some prior knowledge of a relationship between a potential target and a biological condition as claimed.” The experiments and results described in paragraphs 5-12 below support the enablement of the claimed invention by showing clearly that undue experimentation was not required to identify a drug target using the methods of the invention.

5. Illumigen’s first drug is an anti-viral therapy for hepatitis C, and the drug is undergoing important pre-clinical studies; Phase I trials are scheduled for 2007. The drug was developed by following the methods as explicitly described in the present patent application.

6. In Step 1, recruiting of patients was performed from among populations at high risk for hepatitis C infection, specifically intravenous drug users and hemophiliacs. Over 3,500 subjects were screened, and a group of serially exposed and seronegative subjects was identified. These subjects correspond exactly to the ARU “at risk, unaffected” population of the claims and the specification.

7. In Step 2, we sequenced a fraction of the genome of case (ARU) and control (ARA and URU) subjects. These control subjects correspond exactly to the at

risk and affected (exposed to hepatitis C and currently infected with the virus) and unknown risk and unaffected (no exposure data and not currently infected with the virus) populations of the application and claims. Using the computer-based methods exactly as disclosed in the application, genetic association analysis was performed, and a mutation associated with the "at risk and unaffected" ARU group was identified. This mutation affects a protein which corresponds to the "target" of the claims and the specification. Thus, the target was identified solely by the computer-based analysis.

8. The mutation affects a gene involved in the interferon pathway; the gene encodes a protein known as OAS1. Using the information that mutated forms of OAS1 were expressed in the ARU group but not the ARA group, we developed an optimized form of the protein expressed by the mutated gene and tested it in an *in vitro* model of HCV infection; this protein corresponds to the therapeutic of the specification and the claims. As shown in Exhibit 2, the therapeutic protein, referred to as IB657, inhibits EMCV infection of hepatoma (Huh7) cells.

9. On information and belief, the Office Action at page 11, lines 6-8, alleges that "the method of identifying a drug target based on genetic differences between two groups is not trivial and requires years to complete..." Although I agree that identifying a drug target is not "trivial," as it in fact is a major breakthrough, I strongly disagree that it takes years to complete. By following the methods described in this application, we identified a drug target (the mutated gene OAS1) and a drug in three years from start to preclinical drug candidate. A single cycle of data input, review and analysis according to the invention led directly to this drug discovery.

10. On information and belief, the Office Action at page 7, lines 6-10, alleges that "the identification of a drug target requires knowledge of the cause of disease and the biological systems associated with it. Drug target identification currently requires several months to years of research and costs millions of dollars per drug." The operative word here is currently. What applicants have disclosed and claimed is not the current method of target and drug discovery, but new methods. The drug currently

undergoing preclinical testing, as described in paragraph 9 above, was developed at a cost of, at most, 10% of the conventional approach. Furthermore, in addition to the cost benefit, the drug has entirely different toxicity parameters. The drug is based on studying ARU populations who already express a version of the drug and enjoy the beneficial effects of having it in their system. Therefore, the drug we developed is expected to have negligible toxicity compared to traditional drugs based on synthetic chemistry approaches.

11. The drug that is the subject of paragraphs 9 and 10 above is one of many polypeptides disclosed and claimed in our subsequent co-pending patent application, Serial No. 10/972,135. That application was granted Special Status in a Decision on Petition granted on December 7, 2005. The ground for the Petition was that applicant Illumigen is a Small Entity and the subject matter of the application is a major asset of the company.

12. The Small Entity status of the company and the granting of the Petition to Make Special in the co-pending application are further evidence that the present patent application is fully enabling, because the target and the drug were discovered in less than three years through the work of far fewer employees, and using far fewer resources and expenses, as compared to drug discovery at a traditional pharmaceutical company.

I further declare that all statements made herein of my own knowledge are true and that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under § 1001 of Title 18 of the United States Code.

Shawn Iadonato
Shawn Iadonato, Ph.D.

State of Washington)
) ss.
County of King)

On this 2nd day of February, 2006, before me, a Notary Public in and for the State and County aforesaid, personally appeared Shawn Iadonato, Ph.D. to me known and known to me to be the person of that name, who signed and sealed the foregoing instrument, and he acknowledged the same to be his free act and deed.

Shannon Elise Leighton
Notary Public **SHANNON ELISE LEIGHTON**
 MY APPOINTMENT EXPIRES: 5-25-08
Commission expires _____

